

## ORIGINAL ARTICLE

# Left Posterior Approach to the Superior Mesenteric Vascular Pedicle in Pancreaticoduodenectomy for Cancer of the Pancreatic Head

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### ABSTRACT

**Context** Dissection of the superior mesenteric artery is the most important part of a pancreaticoduodenectomy for pancreatic cancer. Since 2005, we have used the left posterior approach for superior mesenteric vascular pedicle dissection, in which the superior mesenteric artery and the superior mesenteric vein are dissected first in a clockwise fashion. **Objective** This article presents the technique of a left posterior approach and the clinical outcome. **Patients** Forty patients underwent a left posterior approach and were compared to 35 patients treated with a conventional dissection. **Main outcome measures** The differences in surgical technique between the left posterior approach and the conventional method were described, and the short- and long-term surgical results compared patients who underwent the left posterior approach to those who were treated with the conventional method. **Intervention** The superior mesenteric vascular pedicle was first dissected from the left lateral border of the superior mesenteric artery. The superior mesenteric vein was also dissected from the left side. Then, the uncinate process and perivascular soft tissue were separated en bloc from the vasculature. **Results** No life-threatening complications occurred after the pancreaticoduodenectomies using a left posterior approach. Diarrhea requiring the administration of antidiarrheal agents occurred in 65% of patients; however, planned adjuvant chemotherapy was completed in all patients who did not have an early tumor recurrence. Survival rate was 52.8% at 3 years after surgery. **Conclusion** After a pancreaticoduodenectomy with a left posterior approach, most patients had various degrees of diarrhea, but the adjuvant chemotherapy was able to be continued with close monitoring. The left posterior approach facilitates understanding of the topographic anatomy in the superior mesenteric vascular pedicle.

### INTRODUCTION

Dissection of the superior mesenteric artery is still the most important part of a pancreaticoduodenectomy for pancreatic cancer. In many institutions, the approach to the superior mesenteric artery is similar, and dissection is performed in the last phase of resection [1, 2, 3]. Recently, Pessaux *et al.* [4] reported a unique method in which the superior mesenteric artery was dissected first. In their method, the margin status of the superior mesenteric artery and the replaced hepatic artery branching from the superior mesenteric artery can be confirmed before resection. The technique required

extensive mobilization of the pancreaticoduodenal portion, but there was no description regarding the exposure and dissection of the distal superior mesenteric artery in their report [4].

Liver metastasis is a major concern in the postoperative follow-up of pancreatic cancer patients [5]; however, an autopsic study has shown that local recurrence is frequently found in patients who died from metastatic disease [6]. Aggressive surgery may not necessarily improve results; however, local tumor control is still important [7, 8, 9].

Since 2005, we have used the left posterior approach for dissection of the superior mesenteric vascular pedicle, in which the superior mesenteric artery and the superior mesenteric vein are dissected first in a clockwise fashion. The superior mesenteric artery is located along the left border of the superior mesenteric pedicle, and the upper jejunal artery or inferior pancreaticoduodenal artery branches off from the sinistral or dorsal aspect of the superior mesenteric artery. The first jejunal vein running behind the superior mesenteric artery is the landmark for the dissection [3]. By first approaching the superior mesenteric artery from the left side, en bloc dissection in the superior mesenteric pedicle and an understanding

Received January 10<sup>th</sup>, 2011 - Accepted March 28<sup>th</sup>, 2011

**Key words** Chemotherapy, Adjuvant; Dissection; Mesenteric Artery, Superior; Pancreatic Neoplasms; Pancreaticoduodenectomy; Surgical Procedures, Operative

**Abbreviations** UICC: Union for International Cancer Control

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of the topographic anatomy for the procedure are facilitated. In cancer surgery, it is a well known that tumors should be resected from as peripheral a site as possible. Furthermore, the surgical margin status to the superior mesenteric artery can be predicted before the pancreaticoduodenectomy. When dissecting the mesenteric pedicle, the surgeon must achieve appropriate cancer clearance and, at the same time, guarantee the safety of the procedure. This article presents our technique of superior mesenteric artery dissection and outlines its clinical outcome.

## MATERIAL AND METHODS

From April 2005 to December 2009, the left posterior approach method was used in 40 patients who underwent a pancreaticoduodenectomy for cancer of the pancreatic head (26 men and 14 women, with a mean age of  $64.0 \pm 9.1$ ). In this period, two other patients who underwent a pancreaticoduodenectomy using the conventional approach were excluded from the analysis. One of these two patients died from cancer recurrence 15 months after surgery, and the other survived for more than 5 years. In contrast, 35 patients underwent a pancreaticoduodenectomy using the conventional approach to the superior mesenteric artery during the 5 year period from January 2001 to May 2005 (20 men and 15 women; mean age:  $65.2 \pm 8.5$  years;  $P=0.635$ , and  $P=0.559$  vs. left posterior approach, respectively). Perioperative and survival data in the left posterior approach group were compared to those in the historical control group. The first author conducted and performed all operations for a total of 75 patients as the first operator ( $n=40$ ) or as the senior surgeon ( $n=35$ ).

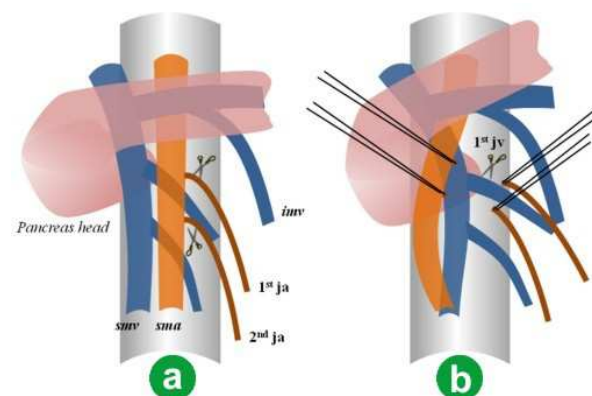
Preoperative jaundice was the first manifestation in 70.0% ( $n=28$ ) of the 40 patients who underwent the left posterior approach. Diabetes mellitus was found in 8 patients (20.0%). No patient received preoperative anticancer chemotherapy or radiotherapy. A pylorus-preserving procedure was performed in 25 patients (62.5%) of the left posterior approach group and in 24 of the control group (68.6%;  $P=0.633$ ). Superior mesenteric-portal vein resection (16/40, 40.0% vs. 13/35, 37.1%; left posterior approach group vs. control group, respectively;  $P=0.817$ ) or retroperitoneal lymph node dissection (28/40, 70.0% vs. 26/35, 74.3%; left posterior approach group vs. control group, respectively;  $P=0.798$ ) were performed producing similar percentages in both groups.

The following pathological findings were determined by routine microscopic examination: tumor differentiation, microvessel invasion, vascular involvement, extent of the tumor and surgical margin status. Lymph node status was classified into three groups: no node metastasis, regional node metastasis and retroperitoneal node metastasis. The regional lymph node was defined based on the Union for International Cancer Control (UICC) TNM classification, but lymph nodes along the distal superior mesenteric artery at the level of origin of the

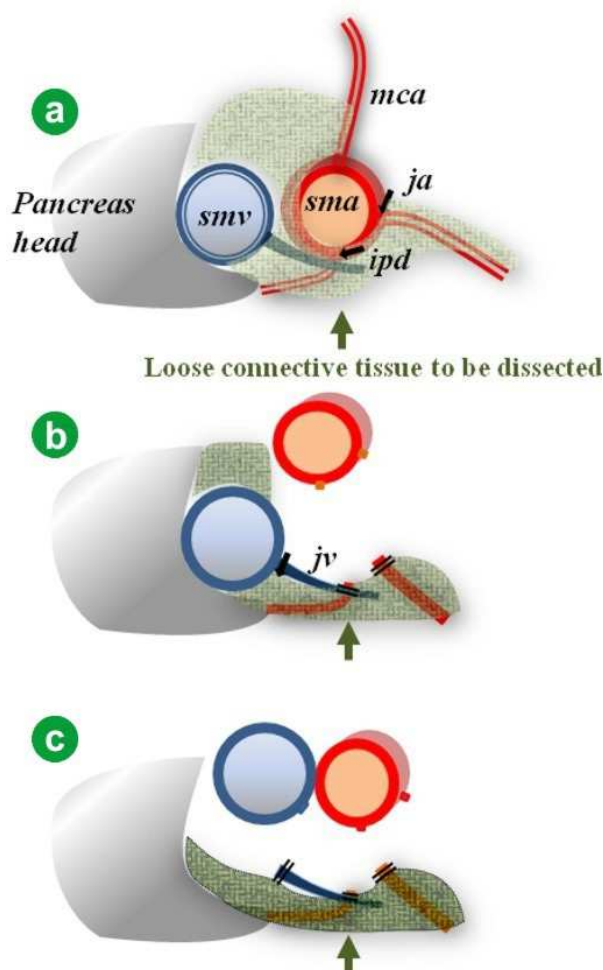
first or second jejunal arteries were included in the regional node group in this study. In addition, cancer invasion of the extrapancreatic nerve plexus (plexus invasion) was included in the R1 category.

## Dissection Technique for the Superior Mesenteric Vascular Pedicle

After laparotomy, the left duodenomesocolic fold is incised, and the retroperitoneum is opened longitudinally. With the transverse colon lifted upward, the pancreatic head and the duodenum are freed from the anterior surface of the inferior vena cava. The thick nerve bundle running down to the right celiac ganglion is found to the right of the superior mesenteric artery. The origin of the superior mesenteric artery covered with loose connective tissue is palpated cephalad to the left renal vein to confirm the end point of the dissection beforehand. After these preparations, the upper jejunum is pulled to the left, and the first and second jejunal arteries are divided at their origin (Figures 1a and 2a). The upper jejunal arteries or the inferior pancreaticoduodenal artery usually arise from the left dorsal aspect of the superior mesenteric artery. The ligament of Treitz is divided. As the upper jejunum is pulled further to the left, the superior mesenteric artery is rotated in a counterclockwise direction. In this way, the posterior and right aspects of the superior mesenteric artery are skeletonized. The first jejunal vein is then uncovered (Figures 1b and 2b). As the inferior part of the pancreatic head and the third portion of the duodenum are moved to the left, the superior mesenteric vein appears behind the superior mesenteric artery. After the division of the first jejunal vein, the superior mesenteric vein can be skeletonized up to its confluence with the splenic vein. Thus, the uncinate process of the pancreatic head is separated from the superior mesenteric vascular pedicle (Figure 2c). After transposing the upper jejunum to the right of the mesenteric pedicle, the loose connective tissue remaining anterior to the superior mesenteric artery is dissected. With this first stage of the procedure, the loose connective tissue around the superior mesenteric



**Figure 1.** Technical illustration of the coronal plane.  
imv: inferior mesenteric vein; ja: jejunal artery; jv: jejunal vein; sma: superior mesenteric artery; smv: superior mesenteric vein



**Figure 2.** Technical illustration of the transverse plane.  
ipd: inferior pancreaticoduodenal artery; ja: jejunal artery; jv: jejunal vein; mca: middle colic artery; sma: superior mesenteric artery; smv: superior mesenteric vein

vascular pedicle is dissected en bloc. Transection of the stomach or duodenum, division of the gastroduodenal artery, and transection of the pancreas are then carried out. The portal vein is skeletonized, and the plexus running along the left celiac ganglion is then dissected. In the second stage, the pancreatic head is completely isolated from the superior mesenteric artery and the celiac axis. Venous reconstruction is conducted at this time, if necessary. In the third stage, the hepatic artery and the portal vein in the hepatoduodenal ligament are skeletonized and dissected. Resection of the gallbladder and bile duct is performed as a final step. In the conventional approach in the control group, dissection of the superior mesenteric artery was performed at the final stage of resection. The neural plexus and the lymph nodes were dissected at the right border of the superior mesenteric artery. The tissue located at the left posterior aspect of the superior mesenteric artery and around the origin of the upper jejunal arteries was not dissected.

The topographic configuration of the jejunal arteries or the nerve plexus in the resected loose connective tissue when using the left posterior approach is presented in

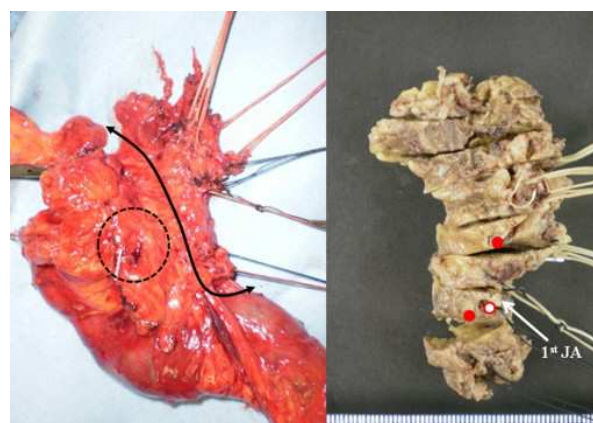
Figure 3 as a case presentation. The mode of tumor infiltration is also traced on its serial step-wise sectioning specimen, in which the widespread microscopic tumor extension is observed (Figure 3).

### Postoperative Adjuvant Chemotherapy

Postoperative adjuvant chemotherapy was given more frequently in the left posterior approach group (n=36, 90.0%) than in the control group (n=24, 68.6%;  $P=0.040$ ). The type of postoperative chemotherapy was divided into two groups as follows: i) gemcitabine-based systemic treatment and ii) combination with liver perfusion chemotherapy using 5-FU *po* or followed by systemic administration of gemcitabine (liver perfusion chemotherapy plus gemcitabine) [10]. In the left posterior approach group, gemcitabine-based therapy was carried out in 19 patients (52.8%) and liver perfusion chemotherapy plus gemcitabine was carried out in 17 patients (47.2%). In the control group, gemcitabine-based therapy was carried out in 18 patients (75.0%) and liver perfusion chemotherapy plus gemcitabine (n=2) or plus 5-FU *po* (n=4) was carried out in total 6 patients (25.0%). Therefore, 56 patients only were treated with gemcitabine out of the 60 patients who had chemotherapy, while a total of 19 patients had no gemcitabine (15 patients had no chemotherapy and 4 patients had liver perfusion chemotherapy plus 5-FU). The type of chemotherapy (gemcitabine-based systemic treatment *versus* liver perfusion chemotherapy) was not significantly different between the two groups of patients ( $P=0.108$ ). The proposed period of treatment with gemcitabine was 6 months or 12 sessions.

### STATISTICS

Data are reported as frequencies and means $\pm$ SD. The Student's *t* test, the Pearson's chi-square test and the Fisher's exact test were used for the analysis. Overall survival curves were generated by the Kaplan-Meier method and compared using the log-rank test. The



**Figure 3.** Case presentation: a fresh surgical specimen (left side) and formalin-fixed connective tissue surrounding the mesenteric pedicle (right side). A focus of plexus invasion (open circle) is located in the vicinity of the first jejunal artery. Metastases to tiny lymph nodes (closed circles) were observed. Loose connective tissue in this figure corresponds to the illustrated tissue in Figure 2c (arrow).

**Table 1.** Comparison of the left posterior approach and the control group regarding postoperative complications.

Analyzed factors	Left posterior approach (n=40)	Control group (n=35)	P value
Pancreatic fistula (grade B or C)	4 (10.0%)	3 (8.6%)	1.000
Intra-abdominal infection	9 (22.5%)	12 (34.3%)	0.308
Intra-abdominal hemorrhage <sup>a</sup>	1 (2.5%)	2 (5.7%)	0.596
Delayed gastric emptying (grade B or C)	7 (17.5%)	16 (45.7%)	0.012
Chylous ascites	2 (5.0%)	-	0.495
Portal vein thrombosis <sup>b</sup>	1 (2.5%)	-	1.000
Stomal ulcer around the duodenojejunostomy	1 (2.5%)	1 (2.9%)	1.000
Re-operation	-	3 (8.6%)	0.097
Operative death or in-hospital death	-	-	-
Diarrhea (required medication)	26 (65.0%)	17 (48.6%)	0.168

Fisher's exact test

<sup>a</sup> Required blood transfusion<sup>b</sup> Due to a plastic tube placed in the portal vein for liver perfusion chemotherapy

median survival rates were reported together with the 95% confidence intervals (95% CIs). Univariate and stepwise multivariate Cox proportional hazards models were applied to identify the significance of the surgical technique on overall survival and hazard ratios; the 95% CIs were also computed. Two-tailed P values less than 0.05 were considered significant. The SPSS 16.0J for Windows was used to carry out the statistical analysis.

## RESULTS

### Perioperative Demographic Data

Mean operative time and blood loss were 516±95 min and 1,307±823 mL in the left posterior approach group, and 526±95 min and 1,352±823 mL in the control group, respectively. The differences were not significant (P=0.651 and P=0.814 for operative time

and blood loss, respectively).

There was no perioperative or in-hospital mortality in either group. The postoperative complications are shown in Table 1. Intra-abdominal hemorrhage occurred in one left posterior approach patient and in two patients in the control group. Heparinization for liver perfusion chemotherapy induced minor hemorrhage at the site of the surgery in one patient in each group. The remaining control patient required re-laparotomy for hemostasis. The incidence of pancreatic fistulae or intraperitoneal infections did not significantly differ between the two groups. Grade B or C delayed gastric emptying decreased to 17.5% (7 patients) in the left posterior approach group as compared to 45.7% (16 patients) in the control group (P=0.012). Chylous ascites in case without infection were observed in two patients who underwent the left posterior approach procedure but were not observed in

**Table 2.** Demographic data of 16 recurrence-free patients who required readmission.

Case	Age/sex	Antidiarrheal agent	Gemcitabine treatment	Reason for readmission	Prognosis
<b>Left posterior approach group</b>					
#1	62/male	No	No	Alcoholism with nutritional and electrolyte disorder	Alive (14 months)
#2	55/male	Yes	Yes	Side effect of adjuvant chemotherapy	Alive (21 months)
#3	77/female	No	Yes	Side effect of adjuvant chemotherapy	Died of disease (8 months)
#4	62/male	Yes	Yes	Side effect of adjuvant chemotherapy and malnutrition	Alive (22 months)
#5	72/female	Yes	Yes	Side effect of adjuvant chemotherapy	Alive (32 months)
#6	58/male	Yes	Yes	Side effect of adjuvant chemotherapy and malnutrition	Alive (33 months)
#7	60/female	Yes	Yes	Side effect of adjuvant chemotherapy and malnutrition	Alive (34 months)
#8	52/male	Yes	Yes	Alcohol abuse and malnutrition	Died of disease (44 months)
#9	80/male	No	Yes	Side effect of adjuvant chemotherapy and femoral neck fracture	Alive (52 months)
#10	66/male	No	Yes	Spinal canal stenosis and pressure cord palsy	Died of disease (18 months)
<b>Control group</b>					
#11	77/female	No	Yes	Femoral neck fracture and pneumonia	Died of another disease (19 months)
#12	65/male	No	Yes	Malnutrition	Died of disease (28 months)
#13	69/female	Yes	Yes	Myocardial infarction	Died of disease (59 months)
#14	73/male	Yes	Yes	Malnutrition	Died of disease (9 months)
#15	65/male	No	No	Alcoholism	Died of disease (46 months)
#16	60/female	Yes	Yes	Side effect of adjuvant chemotherapy	Died of disease (18 months)

**Table 3.** Comparison of pathological features of tumors in the left posterior approach group and the control group.

	Left posterior approach (n=40)	Control (n=35)	P value
<b>Tumor size less than 3 cm</b>	12 (30.0%)	12 (34.3%)	0.805 <sup>a</sup>
<b>Well-differentiated tumor</b>	13 (32.5%)	13 (37.1%)	0.809 <sup>a</sup>
<b>Microlymphatic invasion</b>	27 (67.5%)	30 (85.7%)	0.103 <sup>a</sup>
<b>Microvenous invasion</b>	19 (47.5%)	16 (45.7%)	1.000 <sup>a</sup>
<b>Perineural invasion</b>	34 (85.0%)	33 (94.3%)	0.271 <sup>a</sup>
<b>Invasion to anterior surface membrane</b>	21 (52.5%)	12 (34.3%)	0.162 <sup>a</sup>
<b>Invasion to retropancreatic tissue</b>	33 (82.5%)	28 (80.0%)	1.000 <sup>a</sup>
<b>Invasion to the bile duct</b>	28 (70.0%)	28 (80.0%)	0.427 <sup>a</sup>
<b>Invasion to the duodenum</b>	23 (57.5%)	19 (54.3%)	0.819 <sup>a</sup>
<b>Portal vein invasion</b>	9 (22.5%)	7 (20.0%)	1.000 <sup>a</sup>
<b>Extrapaneatic plexus invasion</b>	11 (27.5%)	7 (20.0%)	0.589 <sup>a</sup>
<b>Lymph node status:</b>			0.747 <sup>b</sup>
- No metastasis	11 (27.5%)	11 (31.4%)	
- Regional node	22 (55.0%)	20 (57.1%)	
- Retroperitoneal node	7 (17.5%)	4 (11.4%)	
<b>Positive surgical margin</b>	11 (27.5%)	10 (28.6%)	1.000 <sup>a</sup>

<sup>a</sup> Fisher's exact test<sup>b</sup> Pearson chi-square

the control group. Reoperation was performed in three patients in the control group due to anastomotic leakage after a partial resection of the colon (n=1), intra-abdominal hemorrhage (n=1) and wound dehiscence (n=1). The overall morbidity, excluding grade B or C delayed gastric emptying, was less in the left posterior approach group (30.0%, n=12) as compared to the control group (42.9%, n=15), but there was no significant difference (P=0.335). The length of the hospital stay after surgery was 45.4±24.0 days in the left posterior approach group and 49.8±15.0 days in the control group, with no significant difference (P=0.352).

The degree of diarrhea after hospital discharge was evaluated by the necessity of antidiarrheal agents. The administration of antidiarrheal agents, such as loperamide hydrochloride or narcotic agents, was required in 26 patients (65.0%) in the left posterior approach group as compared to 17 patients (48.6%) in the control group (not significantly different: P=0.168). During the observation period, a total of 16 recurrence-free patients (10 in the left posterior approach group and 6 in the control group) were rehospitalized (25.0% vs. 17.1%, respectively; P=0.573) (Table 2). Three of the 10 patients in the left posterior approach group (patients #1, #6, and #8) required intensive nutritional support due to their poor nutritional condition. The remaining 7 patients required readmission mainly for treatment of the adverse effects of the chemotherapy. Nutritional status improved after cessation or completion of chemotherapy. All of the patients who did not have early tumor recurrence within 6 months after surgery tolerated the proposed adjuvant chemotherapy.

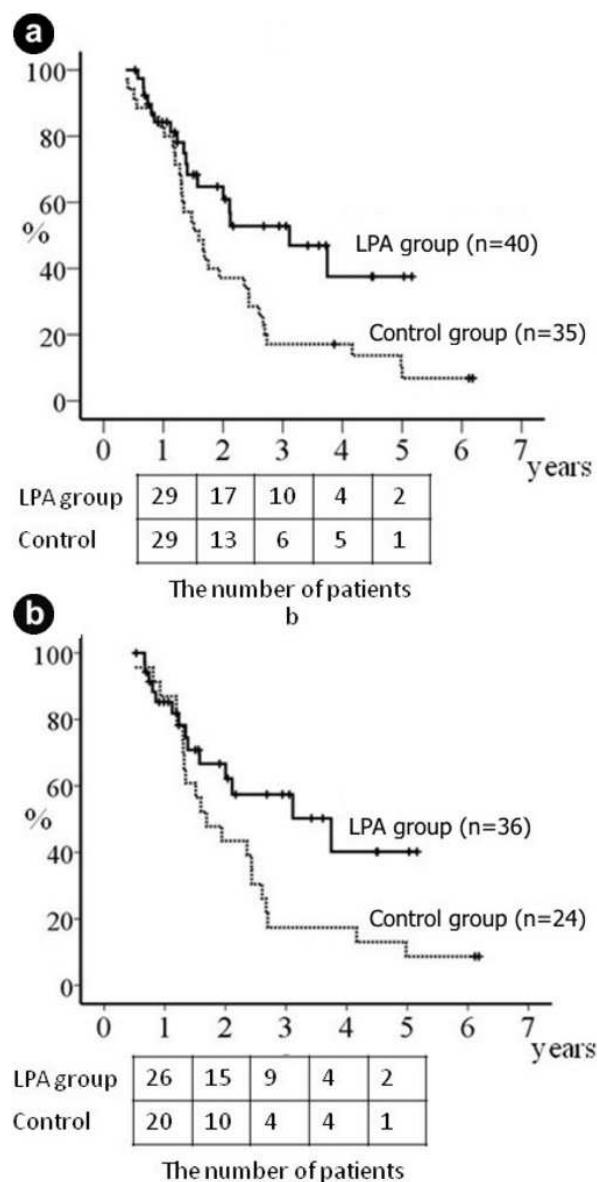
### Pathology

There was no significant difference between the two groups with regard to tumor pathology (Table 3). R1 surgery accounted for 27.5% of the left posterior approach group (n=11) and 28.6% of the control group (n=10) (P=1.000). In two R1 cases in the left posterior approach group, the surgical margin was judged as positive because of lymphatic invasion into the retroperitoneal tissue. In the other 19 patients, the exfoliated surface margin for the superior vascular pedicle was tumor-positive.

### Survival Analyses

In overall survival (Figure 4a), a 3-year survival rate of 52.8% in the left posterior approach group was more favorable than that (17.1%) in the control group (P=0.016). For a total of 75 patients in both groups, the median survival time was 28.3 months (95% CI: 21.4 to 35.1 months) for the 56 patients who were treated with gemcitabine and 16.8 months (95% CI: 14.1 to 19.5 months) for the 19 patients without gemcitabine treatment. The difference in median survival time was statistically significant (P=0.041). When analysis was restricted to patients who received all types of postoperative adjuvant chemotherapy, postoperative survival improved in the left posterior approach group as compared to the control group (P=0.038, Figure 4b). Cox proportional hazards models were applied to identify the significance of the surgical technique on overall survival. Surgical factors with a significant difference, calculated by univariate analysis for dichotomized variables, were surgical technique (left posterior approach or control; P=0.016), postoperative adjuvant chemotherapy (treatment or no treatment; P=0.041), residual tumor (R0 or R1; P=0.002), local tumor extent (T2+T3 or T4 in UICC TNM; P=0.011), lymph node metastasis (negative or positive; P=0.034), and retroperitoneal lymph node metastasis (negative or

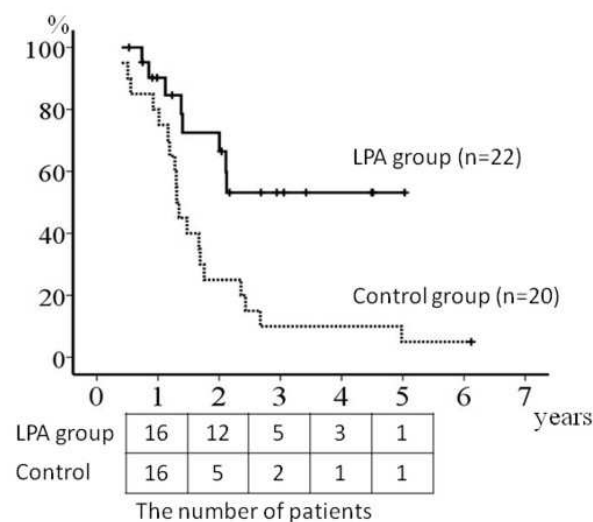




**Figure 4.** Overall survival curves (Kaplan-Meier) for all patients and for patients undergoing adjuvant chemotherapy according to dissection method. **a.** In survival analyses for all patients, 1- and 3-year survival rates were 84.2% (n=29) and 52.8% (n=10) in the left posterior approach (LPA) group and 82.9% (n=29) and 17.1% (n=6) in the control group, respectively. The difference was significant ( $P=0.016$ ). **b.** Even in the subgroup of patients undergoing postoperative chemotherapy, postoperative survival improved in the left posterior approach group (1- and 3-year survival rates: 85.2% (n=26) and 57.5% (n=9), respectively) as compared to the control group (1- and 3-year survival rates: 85.0% (n=20) and 20.0% (n=4), respectively;  $P=0.038$ ). The log-rank test was applied.

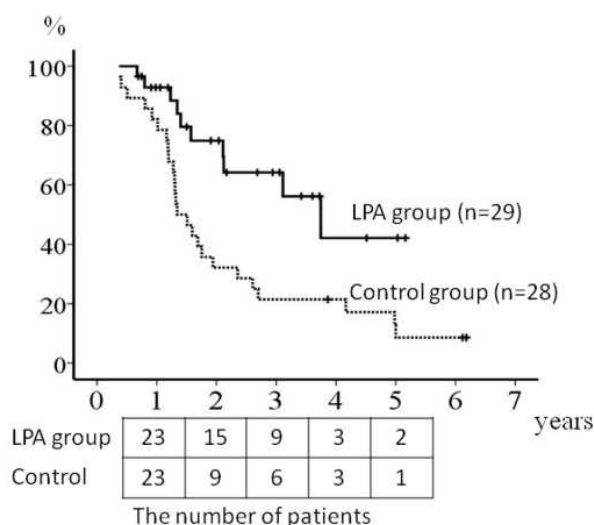
positive;  $P=0.023$ ). Of these factors, R1 factor (HR: 2.60; 95% CI: 1.39 to 4.95;  $P=0.004$ ) and positive retroperitoneal node metastasis (HR: 2.75; 95% CI: 1.31 to 5.76;  $P=0.007$ ) were found to be the only two negative predictors of survival at stepwise multivariate analysis. The left posterior approach was left until the final step of the calculation, but was not identified as a prognostic predictor with a statistical difference ( $P=0.099$ ).

Furthermore, in the patient subgroup having positive regional lymph node metastasis, the survival period



**Figure 5.** Overall survival curves according to dissection method in the positive regional node subgroup. The left posterior approach had a better survival rate as compared to the control group ( $P=0.004$ ). The 1- and 3-year survival rates were 90.2% (n=16) and 53.2% (n=5) in the left posterior approach (LPA) group and 80.0% (n=16) and 16.0% (n=2) in the control group, respectively. The log-rank test was applied.

was significantly longer in the left posterior approach group than in the control group ( $P=0.004$ , Figure 5). However, the dissection technique, either the left posterior approach or the conventional method, had no significant impact on survival in the node-negative subgroup or in the retroperitoneal node-positive subgroup. The subgroup analyses for plexus invasion are shown in Figure 6. In the plexus-negative subgroup, the left posterior approach had a good 3-year survival rate (64.2%) as compared to the controls (21.4%,  $P=0.004$ ). However, there was no significant difference in the plexus-positive subgroup, although



**Figure 6.** Overall survival curves according to dissection method in the negative plexus invasion subgroup. The survival rate was significantly improved ( $P=0.004$ ) in the left posterior approach group (LPA) (1- and 3-year survival rates: 92.8% (n=23) and 64.2% (n=9), respectively) as compared to the control group (1- and 3-year survival rates: 82.1% (n=23) and 21.4% (n=6), respectively). The log-rank test was applied.

one patient in the left posterior approach group has survived for more than 5 years after surgery. With regard to the pattern of recurrence, the overall local recurrence rate was 37.1% (13/35) in the control group, but only 10.0% (4/40) in the left posterior approach group ( $P=0.006$ ).

## DISCUSSION

In pancreatic cancer, resection is the only means of achieving long-term survival, but extensive lymph node dissection tends to be avoided because of impaired activities of daily living or of its small survival benefit [11, 12]. In contrast, the status of the surgical margin is still an important prognostic factor, and local control of the primary tumor is an inherent goal of surgery [7, 8, 9, 13]. In a pancreaticoduodenectomy, dissection of the superior mesenteric vascular pedicle is the most significant part of the procedure for good local control. The most substantial surgical margin is formed from the superior mesenteric artery dissection, and its status is strongly influenced not only by the size or location of the tumor but also by the extent of the dissection [14]. Cancer of the pancreatic head invades the vicinity of the superior mesenteric artery from an early stage [15], and frequently spreads along the inferior pancreaticoduodenal artery [16]. This mode of spread, in which the tumor infiltrates the soft tissue or nerve bundle behind the superior mesenteric vein and superior mesenteric artery, is an important histological feature that we should understand when performing a pancreaticoduodenectomy with curative intent. In resectable tumors of the pancreatic head, the curative effect of pancreaticoduodenectomy seems to be strongly affected by the surgical margin status of the superior mesenteric vascular pedicle. With tumor tissue present less than 1 mm from the microscopic surgical margin, Khalifa *et al.* [14] and Esposito *et al.* [13] defined a distance of less than 1 mm as margin-positive without apparent tumor exposure. Formalin fixation and sectioning of the specimen cause deformation of its shape. Not all aspects of the surgical margin can be diagnosed microscopically. Pathological examination is the gold standard in tumor staging, but it has some limitations, including inter-observer variability and sampling error [17]. It is understandable that a margin of 1 mm enhances the probability of pathological diagnosis for this loose connective tissue. In this study, tumor invasion to the extrapancreatic nerve plexus in the mesenteric pedicle was categorized as margin-positive [18]. We think that perivascular cancer invasion around the superior mesenteric artery involves several patterns of tumor spread; perineural invasion, lymphatic permeation, infiltration into connective tissue and direct invasion of the primary tumor. In perineural invasion, tumor cells are continuously extending along the perineural space from the primary tumor, but a considerable number of serial sectioning specimens are needed for proof. Figure 3 showed a single point of perineural invasion apart from the

primary tumor, with two small metastatic nodes. We could not definitely determine the route of the continuous neural extension of the tumor by microscopic examination using multiple stepwise specimens. In this study, “positive plexus invasion” was categorized as a “positive surgical margin”. Furthermore, the neural plexus and connective tissue surrounding the superior mesenteric artery was more widely dissected in the left posterior approach as compared to the control group, and the detailed microscopic examination which focused on plexus invasion was carried out in the left posterior approach group. For these reasons, it is suggested that the frequency of R1 did not differ between the two groups. Multiple sampling of the nerve plexus during surgery made the true plane of dissection obscure. Extrapancreatic plexus invasion should be considered as a prognostic factor in the same way as lymph node metastasis.

In the commonly used technique for superior mesenteric artery dissection, the tissue to be dissected is pulled to the right, together with the upper jejunum, and the soft tissue to the right of the superior mesenteric artery is resected. The first jejunal vein is approached through a window between the superior mesenteric artery and the superior mesenteric vein. For this reason, the soft tissue must be divided once longitudinally at the right side of the superior mesenteric artery. In the “dissecting the superior mesenteric artery first” technique reported by Pessaux *et al.*, the superior mesenteric artery itself is also approached from the right after extensive kocherization [4]. The first jejunal vein running behind the distal superior mesenteric artery is the landmark in dissection [3], but a description of the vein was not presented in their report [4]. In a recent case-match study, Dumitrascu *et al.* reported that a pancreaticoduodenectomy using the same technique as that described by Pessaux *et al.* [4] reduced both operative blood loss and time [19]. But our study failed to show the advantage of the left posterior approach regarding operative variables. Intraoperative hepatic arterial and portal cannulation for postoperative liver perfusion chemotherapy is thought to influence blood loss and operative time. Intraoperative cannulation was performed in 47% of the left posterior approach group as compared to 17% of the control group. Furthermore, our study included only pancreatic cancer but, in the study reported by Dumitrascu *et al.* [19], half of the patients (10 of 21 patients) had non-pancreatic tumors. In a pancreaticoduodenectomy for pancreatic cancer, inflammation due to obstructive pancreatitis seems to make superior mesenteric artery dissection difficult. On the other hand, Dumitrascu *et al.* stressed that their dissection method provided an early verdict on local resectability for superior mesenteric artery invasion of the tumor [19]. However, not only extensive kocherization but also full mobilization of the right-sided colon was required in their method [4, 19]. We feel that the approach to the first jejunal vein or to the

origin of the first jejunal artery is slightly difficult by their method [4, 19]. In our method, the upper jejunal arteries are first divided at the left border of the superior mesenteric artery. The first jejunal vein is easily identified under the proximal cut stump of the jejunal arteries (Figures 1 and 2). Early detection of superior mesenteric artery or superior mesenteric vein involvement of the tumor and optimal exposure of the replaced or aberrant hepatic artery are well-known advantages common to the "superior mesenteric artery first" approach [4, 19, 20]. In addition, our technique facilitates better understanding of the surgical topographic anatomy for the mesenteric vascular pedicle, including the distal superior mesenteric artery and the superior mesenteric vein. Furthermore, the left posterior approach seems to provide novel technical advantages in terms of performing dissection of superior mesenteric pedicle without mobilization of the duodenum or colon.

In the left posterior approach, the superior mesenteric artery is dissected more than hemi-circumferentially for a length of approximately 6-8 cm from the origin. When the primary tumor extends into the uncinate process, we perform a nearly circumferential dissection. Therefore, approximately 80% of patients required administration of an antidiarrheal agent, but the diarrhea itself was controllable in most cases and did not markedly affect patients' daily activities. The daily activities of patients were impaired by the adverse effects of the adjuvant chemotherapy in addition to the unstable bowel condition. Without tumor recurrence, the patients' condition improved with cessation or completion of the adjuvant chemotherapy. Traverso stresses that margin-negative but less invasive surgery is essential for timely and appropriate adjuvant therapy rather than radical dissection [21]. Indeed, the preservation of the nerve plexus decreases the incidence of intractable diarrhea [22]. In fact, 90% of the patients in the left posterior approach group were able to receive gemcitabine treatment even after aggressive plexus dissection. Chylous ascites were observed in two patients who underwent the left posterior approach procedure, but the intractable lymphorrhea after surgery seemed to decrease with polite ligation and division of the connective tissue containing lymphatic vessels around the mesentery. In this study, the occurrence of grade B/C delayed gastric emptying decreased more in the left posterior approach group than in the control group. A fixed surgical procedure might suppress inflammation of the surgical site and accelerate the recovery of gastric motility. However, we think that the difference in occurrence could be attributed mainly to the difference in postoperative management. Close observation and careful management after surgery are needed, but it seems that aggressive dissection does not always interfere with completing the adjuvant therapy. In several published studies of randomized controlled trials, the 1-year survival rate was 50-60% regardless of the extent of the lymph node dissection [12, 22, 23].

Farnell *et al.* [11] and Yeo *et al.* [24] reported 71-82% and 75% 1-year survival rates, respectively, but in-hospital mortalities were excluded from the survival analyses. In our study, the 1-year survival rate was 83% and the 2-year survival rate was 63% in the left posterior approach dissection group. In general, half of the patients who underwent pancreatic resection had tumor recurrence by 2 years after surgery. The short-term results after surgery seem to be strongly influenced by both tumor stage and surgical curability. Adjuvant chemotherapy appears to be beneficial only in patients who do not show very early tumor recurrence. We think that local tumor control is the first step for long-term survival. In the long-term results, lymph node status and extrapancreatic plexus invasion were significant prognostic factors. In the patient subgroup having positive regional node metastases, the left posterior approach group had an improved survival rate as compared to the control group. It seems that dissection dorsal to the superior mesenteric artery is important for achieving good local tumor control [16]. On the other hand, survival of patients with positive plexus invasion was unaffected by the type of dissection technique. This indicates the technical difficulty of complete resection of tumors extending out of the pancreas along the plexus. Plexus invasion seems to reflect the high malignant potential of the tumor. In most resectable pancreatic cancers, tumor extension to the plexus is confirmed by microscopic examination after surgery. In addition, the remnant tumor in the plexus which was not resected and left cannot be depicted by imaging. The effect of radiotherapy does not seem to be as good as expected. In these cases, it is thought that we should try prolonged administration (one year or more) of gemcitabine-based chemotherapy.

A tumor of the pancreatic head frequently invades the uncinate process, which is fixed to the superior mesenteric artery by the nerve plexus bundle. Superior mesenteric nodes are attached to this plexus. Dissection of the plexus with neighboring lymph nodes appears to be more effective for local control than only lymph node extirpation [25]. Although circumferential dissection of the superior mesenteric artery should be avoided as far as possible, we believe that aggressive surgery to obtain negative surgical margins is still important in surgery for pancreatic cancer. On the other hand, Hirota *et al.* reported that the non-touch isolation technique and extensive intraoperative peritoneal lavage improved the postoperative survival rate [26]. The non-touch isolation technique is an oncological procedure used to prevent hematogenous or lymphogenous metastasis, and early inflow block with this technique decreases intraoperative blood loss in a pancreaticoduodenectomy [27]. However, it appears to be difficult to completely block the outflow drainage from the pancreatic head to the portal vein in the early phase of the operation. While performing the resection, eradicating tumor tissue which may infiltrate into the soft tissue around the pancreas seems to be more



important than preventing intraoperative hematogenous or lymphogenous dissemination of the tumor. Even in resectable pancreatic cancer, postoperative adjuvant therapy is necessary in order to improve surgical outcome. Moreover, gemcitabine treatment is the adjuvant chemotherapy whose antitumor effect was confirmed by a large randomized control trial [28], and the effectiveness of gemcitabine-based chemotherapy was similarly observed in our study. Postoperative survival was favorable in the left posterior approach group as compared to the control group, but definitive conclusions for a survival benefit cannot be drawn because of the retrospective nature of the study. The frequency of adjuvant chemotherapy using gemcitabine differed between the left posterior approach group and the historical control group. However, when survival analysis was restricted to patients who received postoperative gemcitabine treatment, a difference in survival according to surgical technique was observed. A randomized study is needed for confirmation, but the results seemed to indicate the significance of refining the surgical technique to achieve R0 surgery. Touching or incising the tissue which may harbor the tumor should be avoided as much as possible in order to decrease the risk of intraoperative dissemination.

## CONCLUSION

Superior mesenteric artery dissection using the left posterior approach did not impair the short-term survival outcome although the mesenteric nerve plexus was widely resected. In addition, long-term survival was improved in the subgroup of patients with positive regional lymph nodes. This procedure was accompanied by various degrees of diarrhea, but careful monitoring on an outpatient basis allowed administration of standard adjuvant chemotherapy. From a technical point of view, this procedure facilitates the understanding of the topographic anatomy of the superior mesenteric pedicle.

**Conflicts of interest** The authors have no potential conflicts of interest

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